Paper No. 45

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ALBERTO L. MENDOZA

Appeal No. 2003-1819
Application No. 09/082,112

ON BRIEF

Before SCHEINER, MILLS, and GREEN, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 16-25, which are the claims on appeal in this application.

Claims 16, 18 and 19 are illustrative of the claims on appeal and appear below.

16. A method for treatment of Pythiosis in human patients having the Pythiosis which comprises:

(a) providing a vaccine containing a mixture of mixed intracellular proteins and mixed extracellular proteins of *Pythium insidiosum* in a sterile aqueous solution, wherein the mixed intracellular proteins, which consist essentially of proteins removed from disrupted cells of the *Pythium insidiosum* grown in a culture medium, and the mixed extracellular proteins, which consist essentially of proteins removed from the culture medium for growing *Pythium insidiosum*, are in water and the mixture has been dialysed to remove molecular weight components less than 10,000 MW; and

(b) vaccinating the patient with the vaccine.

18. A method for the treatment of Pythiosis in a mammal having the Pythiosis which comprises:

(a) providing an injectable vaccine derived from growing cells of *Pythium insidiosum* in a culture medium which comprises in a sterile aqueous solution in admixture:

(1) mixed intracellular proteins, which consist essentially of proteins removed from disrupted cells of the *Pythium insidiosum* separated from the culture medium; and

(2) mixed extracellular proteins, which consist essentially of proteins removed from the culture medium separated from the cells of the *Pythium insidiosum*;

wherein the admixture in water has been dialyzed to removed low molecular weight components less than 10,000 MW to produce the vaccine; and

(b) vaccinating the mammal with the vaccine.

19. The method of claim 18 wherein the removed proteins in the admixture have been provided by growing cells of the *Pythium insidiosum* in the culture medium, then killing the cells, then separating the killed cells from the culture medium to produce a first supernatant to provided the mixed extracellular proteins of (a)(2) and then disrupting the killed cells in sterile water and removing the disrupted cells from the sterile water containing the mixed intracellular proteins to provide the mixed intracellular proteins of (a)(1) in a second supernatant, combining the first and second supernatants, precipitating the proteins, resuspending the precipitated proteins in sterile water, and dialyzing the resuspended proteins in sterile water to remove the material less than 10,000 MW.

The prior art references cited by the examiner[1] are:

Mendoza et al (Mendoza 1996), J. Mycol. Med. Vol. 6, pp. 151-164 (1996)

Mendoza et al. (Mendoza 1992a), Mycopathologica, Vol. 119, pp. 89-93 (1992)

Mendoza et al. (Mendoza 1992b), J. Clin. Microbiol., pp. 2980-2983 (1992)

Mendoza et al. (Mendoza 1995), Third NIAID Workshop in Medical Mycological Series (Abstract), Sept. 7-9 (1995)

Sigma Catalog, p. 1874 (1992)

Amicon Catalog, p. 35 (1993)

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[1] For ease of reference to the Answer, we adopt the Examiner's reference naming scheme.

Grounds of Rejection

Claims 19 and 24 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite.

Claims 16-25 stand rejected under 35 U.S.C. §103, as obvious over Mendoza 1996, Mendoza 1992a, Mendoza 1992b, Mendoza 1995, Sigma Catalog and Amicon Catalog.

We reverse the rejection of claims 19 and 24 under 35 U.S.C. §112, second paragraph, as indefinite. We affirm the rejection of claims 16-25 under 35 U.S.C. §103, as obvious over Mendoza 1996, Mendoza 1992a, Mendoza 1992b, Mendoza 1995, Sigma Catalog and Amicon Catalog.

Claim Grouping

According to appellant, 16 and 17 stand or fall together for the rejection under 35 U.S.C. §103. Brief, page 7. Claims 19 and 24 are grouped together with respect to the rejection under 35 U.S.C. §112, second paragraph. We select claims 16 and 19 as representative of each rejection, respectively. 37 CFR 1.192(c)(7) (2003).

DISCUSSION

35 U.S.C. §112

Claims 19 and 24 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite.

It is the examiner's position that the phrase, "removing the disrupted cells to provide the mixed intracellular proteins" in claims 19 and 24, is indefinite. Answer, page 3. The examiner argues that one of ordinary skill in the art would not know what is being removed or what steps are being performed. The examiner surmises that, "Appellants appear to be referring to the removal of insoluble cellular material via centrifugation and removal of the supernatant with discarding of the pellet. Yet the artisan does not readily recognize how removal of disrupted cells may be achieved and therefore the recited step is indefinite as to what step is being performed and its subsequent effect on the vaccine prepared by the recited method." Answer, pages 3-4.

Appellant responds, arguing that, "the most common method for removing the disrupted killed cells is centrifugation and that after centrifugation, the supernatant fraction would contain the mixed intracellular proteins. Furthermore, to provide guidance to one of ordinary skill in the art, the applicant teaches in Example 1 disrupting the killed cells in sterile water by sonication and then removing the killed cells by centrifugation." Brief, page 8. According to the Answer, the examiner also appears to have reasonably understood the claim as referring to a centrifugation method and the product resulting from performance of a centrifugation method. Thus, we agree with appellant, that when the claims are read in view of the specification, one of ordinary skill in the art at the time of the invention would have been able to discern the claim scope.

In view of the above, we reverse the rejection of claims 19 and 24 under 35 U.S.C. §112, second paragraph.

35 U.S.C. §103

Claims 16-25 stand rejected under 35 U.S.C. §103, as obvious over Mendoza 1996, Mendoza 1992a, Mendoza 1992b, Mendoza 1995, Sigma Catalog and Amicon Catalog.

According to the examiner, Mendoza 1992a discloses two prior art Pythium insidiosum vaccines, a cell-mass vaccine (CMV)[2] and a soluble concentrated antigen vaccine (SCAV).[3] Answer, page 4.

The examiner acknowledges that neither of the CMV or SCAV vaccines of Mendoza et al., 1992a are the vaccines as disclosed in Example 1 of the specification, as "neither of the prior art vaccines has isolated cytoplasmic antigens added to the preparations." Paper No. 32, page 4. The examiner, however, acknowledges that specification, Example 1 references that the prominent cytoplasmic antigens added to Mendoza's original vaccine[4] (SCAV vaccine) were as described in Mendoza 1992b. Id.

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[2] Appellant characterizes the CMV of the prior art as an intracellular protein vaccine. Brief, page 10. Appellant characterizes the SCAV vaccine of the prior art as an extracellular protein vaccine. Id.

[3] Based on the guidance in Example 1 of the specification, the examiner understands that for the claimed vaccine, isolated antigens were added to the vaccine of Mendoza's earlier publication in 1986 which corresponds to the SCAV vaccine. Paper No. 32, page 4.

[4] Mendoza's original vaccine is defined in the specification as composed of culture filtrated antigens, and is later referenced in Mendoza 1992b. Specification, page 3.

Significantly, in support of the rejection the examiner relies on Mendoza 1995 which teaches the addition of the 28-32 kD (intracellular) immunodominant peptides (from CMV) to culture filtrate proteins (SCAV) leads to the cure of 8 infected horses. Answer, page 4. Thus, it would reasonably appear that Mendoza 1995 describes that specific, prominent cytoplasmic intracellular antigens of Mendoza 1992b were added to the SCAV vaccine (mixed extracellular preparation). Answer, page 4. The addition of these intracellular cytoplasmic antigens described in Mendoza 1992b to the SCAV as described in Mendoza 1995 provides for an improved vaccine which cures chronically infected horses. Answer, page 4.

The examiner understands that the vaccine of Mendoza 1995 is "different from the vaccine claimed in that the claimed vaccine is essentially a combination, a vaccine which combines the elements of the CMV and SCAV preparations (mixed intracellular and mixed extracellular proteins) of the prior art" whereas the vaccine of Mendoza 1995 is a mixture of specific isolated antigens from the CMV added to the SCAV. Paper No. 32, page 5. Mendoza 1996 is relied on by the examiner for its indication of the similarity in human and animal Pythiosis infections, and that the same immunodominant antigens were recognized in both horse and human sera. Answer, page 7. From this evidence, the examiner submits that one of ordinary skill in the art would expect beneficial results of the vaccine in humans.

The examiner finds that the (Answer, page 5)

> suggestion of the prior art is that the combination of mixed intracellular and extracellular proteins provide the enhanced curative properties to chronically infected horses. In addition, upon such teaching, the combination of the CMV (containing the immunodominant proteins) and the SCAV (mixed extracellular) proteins would have been prima facie obvious to the artisan, particularly in that the combination of the two preparations would provide the required constituents yet would be easier in preparation than providing only the isolated immunodominant proteins because there would be no need for the additional preparative steps including isolation of the 28-32 kD antigens via gel electrophoresis recovery from the gel and addition to the SCAV vaccine.

We agree that the examiner has established a prima facie case of obviousness. In our view the mixed intracellular proteins of the claimed vaccine read on the mixture of 28-32 kD immunodominant proteins of Pythium insidiosum described in the prior art vaccine of Mendoza 1995.[5]

Where the prior art, as here, provides a reason suggestion or motivation to make the claimed invention, the burden then falls on an appellant to rebut that prima facie case. Such rebuttal or argument can consist of any other argument or presentation of evidence that is pertinent. In re Dillon, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (en banc), cert. denied, 500 U.S. 904 (1991).

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[5] In an alternative, acceptable theory of the prima facie case, the examiner suggests that one of ordinary skill in the art would have been motivated to substitute the CMV of Mendoza 1992b for the 28-32 kD immunodominant proteins of the vaccine of Mendoza 1995 with an expectation of success because the immunodominant proteins of Mendoza 1995 "are present in the CMV preparation." Answer, page 11

Appellant would appear to acknowledge that the CMV vaccine of the prior art is an intracellular protein vaccine, and the SCAV vaccine is an extracellular protein vaccine. Brief, page 10. Appellant also acknowledges that Mendoza 1995 discloses "an SCAV vaccine containing three immunodominant intracellular proteins." Brief, page 12. Appellant argues that even so, the prior art does not suggest to a person of ordinary skill in the art to make a vaccine that contain all the soluble intracellular proteins (but not the insoluble proteins) and the extracellular proteins. At best, one of ordinary skill in the art would most likely be motivated to make a vaccine consisting of the SCAV and the three immunodominant proteins." Brief, page 13.

The examiner responds, arguing that the presence of, "[a]ll of the intracellular proteins are not required by the claims." Answer, page 12. The examiner further argues that, "the elements of the claimed invention, i.e., mixed intracellular and mixed extracellular proteins are provided and are within the scope of the claim regardless of whether all of the intracellular antigens or merely the immunodominant intracellular antigens are provided." Id. We agree with the examiner's claim interpretation, and find that the claims before us do not require all of the intracellular proteins of the CMV, only a mixture of these proteins. Nor do the claims specifically require only soluble intracellular proteins with the exclusion of all insoluble proteins, as argued by appellant.

Appellant argues that there is nothing in the Mendoza references cited which would suggest to one of ordinary skill in the art that adding only the soluble intracellular proteins of the CMV to the SCAV would produce a vaccine with an efficiency superior to

either prior art vaccine and which would not have the undesirable attributes of CMV. Brief, page 14. However, we agree with the examiner that the claims are not limited to only the soluble intracellular proteins of the CMV. The claims recite "(1) mixed intracellular proteins, which consist essentially of proteins removed from disrupted cells of the Pythium insidiosum separated from the culture medium." There is no indication in the specification or otherwise, that the mixed intracellular protein of the specification does not contain any soluble protein material, or that the inclusion of insoluble protein material would affect the basic and novel characteristics of the claimed subject matter.[6]

The examiner further submits that there is no comparative data of record which demonstrates different or unexpected effects which are attributed to a preparation containing all the intracellular proteins in comparison to one containing only the immunodominant peptides. Answer, page 12. To this end we acknowledge that Mendoza 1995 describes the enhancement of the therapeutic effect of the SCAV vaccine by adding the hyphal proteins of Pythium insidiosum. See Title, p. 9. It would reasonably appear that an enhanced or superior result would have been expected from a vaccine comprising the immunodominant proteins of the CMV described in Mendoza 1995 and additional intracellular proteins of the CMV. Expected beneficial results are evidence of obviousness just as unexpected beneficial results are evidence of

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[6] The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. In re Herz, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976).

unobviousness. See In re Skoner, 517 F.2d 947, 950, 186 USPQ 80, 82 (CCPA 1975).

Next, Appellant argues that "unlike the applicant's vaccine, both vaccines made in view of the prior art would contain material less than 10,000 MW." Id. According to appellant, the composition of Mendoza 1992a, containing soluble intracellular proteins, further includes material less than 10,000 MW and insoluble proteins. Brief, page 14.

The examiner responds, arguing, "the method/process limitations of filtration via ultracentrifugation or a stir cell through a PM-10 membrane remove small peptides and impurities as ... evidenced by ... Amicon catalog p. 35. Again a stir cell removes small constituents with a molecular weight less that [sic] 10,000MW. The small constituents flow through the membrane with the wash fluid. This step is an obvious equivalent which does not appear to result in a patentably distinguishable product from that of dialysis to remove small peptides and impurities because the molecular weight cut offs for the PN-10 membrane and a dialysis membrane are similar as evidenced by Sigma, Amicon and Mendoza et al., 1992(b). Sigma teaches dialysis tubing with a molecular weight cutoff of approximately 12,400 MW and PM-10 membrane of MW cut-off of 10,000 MW."

In our view, Appellant has failed to sufficiently respond to the examiner's evidence that claimed dialysis MW cut offs and the prior art filtration cutoffs are equivalent. Answer, page 13. Appellant continues to argue that the claimed method "steps and the order they are performed produces a vaccine which is not equivalent to a mixture of either the CMV and the SCAV or the intracellular protein preparation in

Mendoza (1992b) and the SCAV", but fails to explicitly explain a difference in the two. Reply Brief, page 8.

This argument of appellant is mere attorney argument which is unsupported by evidence. Appellant is reminded that arguments of counsel cannot take the place of evidence. In re DeBlauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984), In re Payne, 606 F.2d 303, 315, 203 USPQ 245, 256 (CCPA 1979). In addition, appellant's Example 1, specification, page 6, admits that "the improved vaccine was prepared by adding cytoplasmic antigens to the earlier *P. insidiosum-vaccine* (Mendoza et al., Mycopathological 119:89-95 (1992)." Appellant has presented no evidence indicating a difference in the earlier *P. insidiosum-vaccine* of the prior art, Mendoza 1992a, and the mixed extracellular product claimed.

In view of the above, we do not find appellant has put forth sufficient argument or evidence to rebut the examiner's prima facie case of obviousness. The rejection of the claims for obviousness is affirmed.

CONCLUSION

The rejection of claims 19 and 24 under 35 U.S.C. §112, second paragraph, as indefinite is reversed.

The rejection of claims 16-25 under 35 U.S.C. §103, as obvious over Mendoza 1996, Mendoza 1992a, Mendoza 1992b, Mendoza 1995, Sigma Catalog and Amicon Catalog is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

TONI R. SCHEINER
Administrative Patent Judge

DEMETRA J. MILLS
Administrative Patent Judge

LORA M. GREEN
Administrative Patent Judge

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